Faculty of Science
Biochemistry Department

Evaluation of the Therapeutic Potential of Bone Marrow Derived-Mesenchymal Stem Cells in an Experimental Model of Lung Fibrosis

A thesis submitted for the degree of Ph.D. in Biochemistry

Submitted by

Alyaa Saher Abd El Halim

(M.Sc. in Biochemistry 2015)
Assistant Lecturer of Biochemistry - Faculty of Science - Ain Shams University

Under the supervision of

Prof. Dr. Mohamed R. Mohamed

Professor of Biochemistry & Molecular Biology
Faculty of Science
Ain Shams University

Prof. Dr. Hanaa H. Ahmed

Professor of Biochemistry
Hormones Department
Medical Research Division
National Research Centre

Dr. Hadeer A. Aglan

Researcher of Biochemistry
Hormones Department
Medical Research Division
National Research Centre

Faculty of Science
Ain Shams University
2020

سورة البقرة الآية: ٣٢

This thesis has not been submitted before to this or any other University

Alyaa Saher Abd El Halim

ACKNOWLEDGEMENT

No words can express my sincere gratitude to ***Prof. Dr. Mohamed Ragaa Mohamed***, for his meticulous supervision, sincere guidance, constructive suggestions and wholehearted moral support throughout this work.

Special thanks are extended to ***Prof. Dr. Hanaa Hamdy Ahmed***, for giving me the privilege of working under her valuable supervision, for her constant support and fruitful comments at every stage of this work.

I owe my sincere thanks and gratitude to ***Dr. Hadeer Ahmed Ahmed Aglan***, for her kind supervision, great support, instructive guidance, valuable technical assistance and helpful advice.

I also express my sincere appreciation to ***Prof. Dr. Adel Bakeer Kholoussy***, Professor of Pathology, Faculty of Veterinary Medicine, Cairo University, for his kind cooperation in conducting histological examination.

Alyaa Saher Abd El Halim

Contents

List of abbreviations

Abbreviations	Full name
ABM	Alveolar basement membrane
ACTB	β-actin
AD	Amiodarone
AEC1	Type 1 alveolar epithelial cells
AEC2	Type 2 alveolar epithelial cells
AECs	Alveolar epithelial cells
AMSCs	Adipose tissue-derived mesenchymal stem cells
Ang1	Angiopoietin 1
ANOVA	One-way analysis of variance
ASCs	Adult stem cells
BAL	Bronchoalveolar lavage
BLM	Bleomycin
BM-MSCs	Bone marrow-derived mesenchymal stem cells
CC16	Clara cell secretory protein
CCL	Chemokine (C-C motif) ligand
CCR	C-C chemokine receptor type
CD	Cluster of differentiation
cDNA	Complementary DNA
CM	Conditioned media
COL1A1	Type I collagen
COPD	Chronic obstructive pulmonary disease
CTGF	Connective tissue growth factor
CXCL	C-X-C motif chemokine ligand
CXCR	C-X-C chemokine receptor
DL_{CO}	Diffusing capacity of lungs for carbon monoxide
DMEM	Dulbecco's Modified Eagle's medium
ECM	Extracellular matrix
EGFR	Epidermal growth factor receptor
ELISA	Enzyme-linked immunosorbent assay

EMT	Epithelial to mesenchymal transition
EP2	Prostaglandin E2 receptor 2
EP4	Prostaglandin E2 receptor 4
EPCs	Endothelial progenitor cells
ER	Endoplasmic reticulum
ESCs	Embryonic stem cells
EVs	Extracellular vesicles
FBS	Fetal bovine serum
FGF	Fibroblast growth factor
FITC	Fluorescein isothiocyanate
FVC	Forced vital capacity
G-CSF	Granulocyte colony stimulating factor
GM-CSF	Granulocyte/macrophage colony stimulating factor
GSK	Glycogen synthase kinase
H&E	Hematoxylin and eosin
HAECs	Human amniotic epithelial cells
HGF	Hepatocyte growth factor
HO-1	Hemeoxygenase 1
HRCT	High-resolution computed tomography
HRP	Horseradish peroxidase
HSC	Hematopoietic stem cell
IDO	Indoleamine 2,3-dioxygenase
IGF-1	Insulin like growth factor 1
IL	Interleukin
IL-1Ra	Interleukin 1 receptor antagonist
IPF	Idiopathic pulmonary fibrosis
iPSCs	Induced pluripotent stem cells
IQR	Interquartile range
JNK	c-Jun N-terminal kinase
KGF	Keratinocyte growth factor
LIF	Leukemia inhibitory factor
L-MSCs	Lung mesenchymal stem cells
MCP-1	Monocyte chemoattractant protein 1
MIP-2	Macrophage inflammatory protein 2
MMP	Matrix metalloproteinase

MPCs	Mesenchymal progenitor cells
MSCs	Mesenchymal stem cells
NF-κB	Nuclear factor kappa light chain enhancer of activated B cells
NK	Natural killer cells
OD	Optical density
PAH	Pulmonary arterial hypertension
PBS	Phosphate-buffered saline
PDGF	Platelet derived growth factor
PF	Pulmonary fibrosis
PGE2	Prostaglandin E2
PKC	Protein kinase C
PLL	Poly-L-lysine
PS	Phosphatidylserine
qPCR	Quantitative real-time polymerase chain reaction
RT	Reverse transcription
S100A4	S100 calcium-binding protein A4
SD	Standard deviation
SDF-1	Stem cell derived factor-1
SMAD	Mothers against decapentaplegic homolog
STC-1	Stanniocalcin 1
TGF-β1	Transforming growth factor beta 1
TIMP	Tissue inhibitor of matalloproteinase
TNF-α	Tumor necrosis factor-α
TSG-6	Tumor necrosis factor-stimulated gene 6
uMSCs	Umbilical cord mesenchymal stem cells
VEGF	Vascular endothelial growth factor
α-SMA	Alpha-smooth muscle actin

List of figures